Remarks

Claims 1 to 13 were in the application as filed. Claims 14 to 22 were added in the Preliminary Amendment filed on December 22, 1999. Claim 8 was canceled by the Amendment filed on October 23, 2003.

Applicants have fully considered the rejections raised by the Examiner. Applicants are of the opinion that Claims 1 to 7 and 9 to 22, prior to the instant amendments, meet the patentability criteria over the prior art. Nevertheless, at the current stage of the procedure and in order to secure allowance of the patent, Applicants have amended the claims as explained below to more particularly describe the present invention. Entry of these amendments is respectfully requested.

Claim 1 has been amended as follows: the solid composition for oral administration is limited to tablet forms (support for this amendment can be found in the specification, for example, on page 3, line 37 and in the examples); the nonionic hydrophilic surfactant is selected from poloxamers (support for this amendment can be found in the specification, for example, on page 4, line 7 and in the examples); and the proportion of nonionic hydrophilic surfactant, expressed by weight of the active principle in base form, is changed to 5 to 15% (support for this amendment can be found in the specification, for example, on page 4, lines 36-37 and in the examples).

Claims 6, 12, and 13 have been amended to essentially incorporate the above-described amendments to Claim 1 therein. Claim 18 has been amended and Claims 5, 9, 10 and 17 have been canceled to remove redundant claims.

No new matter had been added by these amendments.

As presently amended, Claims 1 to 4, 6 to 7, 11 to 16, and 18 to 22 are pending in this application.

Obviousness Rejections

Claims 1 to 7 and 9 to 22 are rejected under 35 U.S.C. § 103(a) as being, the Examiner alleges, unpatentable over the Physician's Desk Reference ("PDR") in view of US Patent No.

4,994,949, issued to Story et al. ("Story et al.") and Martin-Algarra et al., International Journal of Pharmaceutics, 122 (1995), pp. 1-8 ("Martin-Algarra").

This rejection is traversed and reconsideration and withdrawal thereof are respectfully requested for the reasons given hereinbelow.

The aim of the instant invention is to provide a solid pharmaceutical composition for oral administration containing a benzofuran derivative with antiarrhythmic activity as active principle, such as amiodarone and dronedarone. The formulation of such a benzofuran derivative was a challenge given its low solubility in aqueous medium, particularly in the intestine medium (neutral medium), and given its variability of absorption depending on the intake of food (see Specification at page 1, line 36 to page 3, line 12).

Referring to the prior art cited by the Examiner, the PDR teaches the low solubility of amiodarone. For other types of poorly soluble active principles, namely non-steroidal anti-inflammatory drugs (NSAIDs), Story *et al.* teach the addition of surfactants to a formulation:

- which is in liquid form (see column 4, lines 39-58 and the examples, which all relate to solutions or to liquid-filled capsules); and
- which contains a far greater content of the surfactant compared to the active principle (see column 12, lines 56-61: the surfactant is used at a 5.7 to 50 fold greater amount than the active principle).

Story *et al.* therefore provides no guidance to one skilled in the art searching for a solid pharmaceutical composition in tablet form. Furthermore, even though Story *et al.* mention poloxamers among numerous surfactants available in pharmaceutical science (enumerated through columns 5 to 7), *none* of the specific formulations exemplified by Story *et al.* (examples 1 to 127, columns 12 to 22) use poloxamer surfactants, thereby deterring one skilled in the art from using such surfactants. Accordingly, Story *et al.* provides no motivation to choose a poloxamer surfactant, as recited in presently amended claim 1.

Therefore, even if one of skill in the art combined the PDR and the Story *et al.* teachings, they would not arrive at the invention as recited in presently amended claim 1, wherein the composition is in the form of a tablet *and* wherein the quantity of surfactant is 5-15% by weight of the active principle *and* wherein the surfactant chosen is a poloxamer.

The third reference cited by the Examiner, Martin-Algarra, similarly fails to address the problem of providing a composition for oral administration, as only an *in situ* rat gut technique is taught. Even assuming that one skilled in art would look to the teachings of Martin-Algarra to prepare a composition for oral administration (which they would not), they would only be motivated to use polysorbate 80 (which is the surfactant used in this document in combination with amiodarone), instead of poloxamers as required by presently amended claim 1 of the instant invention.

It is therefore apparent that, first, there is no suggestion or motivation to modify the three prior art references analyzed above or to combine them; second, there could not be a reasonable expectation of success since neither Story *et al.* nor Martin-Algarra *et al.* address the problem of providing a solid pharmaceutical composition in tablet form; and finally, the prior art references do not teach nor suggest all of the features now recited in presently amended claim 1.

The solid pharmaceutical compositions in tablet form for oral administration as recited in presently amended claim 1 are, therefore, non-obvious over the prior art references.

Claims 2, 7, 11, 12, 16 and 18 to 22 are rejected under 35 U.S.C. § 103(a) as being, the Examiner alleges, unpatentable over Martin-Algarra.

This rejection is traversed and reconsideration and withdrawal thereof are respectfully requested for the reasons given hereinbelow.

As stated above, Martin-Algarra fails to teach or suggest a pharmaceutical composition in tablet form for oral administration of a benzofuran derivative, or the use of a poloxamer surfactant in such a composition. Additionally, Martin-Algarra fails to provide the requisite "reasonable expectation of success" for preparing a pharmaceutical composition in tablet form for oral administration of a benzofuran derivative. Accordingly, the rejection of Claims 2, 7, 11, 12, 16 and 18 to 22 should be withdrawn.

Double Patenting Rejection

Claims 1 to 7 and 9 to 22 are rejected under the judicially created doctrine of obviousness-type double patenting as being, the Examiner alleges, unpatentable over claims 1 to 30 of US Patent No. 6,143,778. The Examiner acknowledges that there is nothing in US

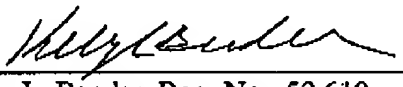
6,143,778 to suggest lyophilizing the composition in the patent, but the Examiner nevertheless concludes that "to incorporate said liquid composition into a capsule capable of containing liquid for oral administration would have been obvious." (Office Action page 4).

In view of the above-described amendments to Claim 1, limiting the invention to compositions in the form of tablets, this objection is believed overcome and withdrawal thereof is respectfully requested.

There being no remaining issues, this application is believed in condition for favorable reconsideration and early allowance, and such actions are earnestly solicited.

The Commissioner is hereby authorized to charge any additional fees which may be required by this paper, or credit any overpayment to Deposit Account No. 18-1982.

Respectfully submitted,



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